REMARKS

Claims 1-23 were originally filed in this application. Claims 9, 10, and 22 were previously withdrawn from consideration as being drawn to a nonelected invention and claims 13-20 and 23 were previously cancelled. In this response, claims 1, 11, and 12 have been amended. No claims have been cancelled or added. Support for the amendment is found throughout the specification as originally filed. No new matter has been added. Accordingly, claims 1-8, 11, 12, and 21 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Claim Rejections-35 U.S.C. § 112

A. Claims 1-8, 11-12, and 21 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the final Office Action states that the term "non-aerosol" lacks literal support in the specification as originally filed.

Without acquiescing to the rejection, and to expedite prosecution, independent claims 1 and 11 have been amended to remove the term "non-aerosol." Accordingly, withdrawal of the written description rejection of claims 1 and 11, and claims that depend therefrom is respectfully requested.

B. Claims 12 and 21 stand rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Specifically, the final Office Action states that claim 12, which depends from claim 11, is drawn to administration of sprays and aerosolized or

mobilized particles, which is contradictory to the "non-aerosol" formulation recited in the claim from which it depends.

The rejection is rendered moot by the amendment to claim 12 that removes the reference to sprays and aerosolized or nebulized particles. Given that claim 21 does not contain such a reference, it is believed that the rejection with respect to claim 21 was inadvertently made in error. Appropriate correction is requested.

Claim Rejections-35 USC §103(a)

Claims 1-8, 11, 12, and 21 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Biesalski (U.S. 5,556,611) in view of Belloni (6,339,107). Specifically, the final Office Action states that Biesalski teaches an aerosol formulation having the claimed range of retinoic acid that is effective for treating disturbances and impairments of mucous membranes, including respiratory epithelium. The final Office Action further states that Biesalski does not expressly teach a depot formulation of retinoic acid or a cause of ciliated epithelial structure damage due to surgical intervention, but that it would have been obvious to one of skill in the art to modify the aerosol formulation of Biesalski to a topical depot formulation as taught by Belloni. This is because Belloni discloses that retinoic acid can be formulated as gels, ointments, creams, suspensions, etc., and that retinoic acid is effective for the treatment of impaired ciliated epithelium regardless of cause.

Applicants strongly disagree that obviousness has been established because Belloni teaches away from using retinoic acid in its formulations. Retinoic acid is also known as all-trans-retinoic acid (ATRA) (Merck Index, 14th Edition, p. 1407). Belloni teaches that the use of ATRA in treating emphysema is undesirable because the compound presents several toxicity concerns (column 2, lines 61-64). Furthermore, Belloni provides data in Table 6 (top of column 15) that demonstrates the higher therapeutic index of 13-cis-retinoic acid as compared to ATRA. In explaining the data at column 15, lines 40-53, Belloni states:

> "...ATRA is substantially less effective than 13-cis-retinoic acid in repairing alveoli at low dosages. Thus, although the efficacy of ATRA and 13-cis-retinoic acid are similar at high dosages, 13-cis-retinoic acid is considerably safer than ATRA, because unlike ATRA, it does not elevate triglycerides even at high dosages and it [*sic*] also efficacious at low dosages at which ATRA is ineffective. Thus, the therapeutic index of 13-cis-retinoic acid for treating emphysema is surprisingly more favorable when compared to the therapeutic index for treating ATRA. Finally, the data also show that ATRA, unlike 13-cis-retinoic acid, does not have a statistically significant therapeutic effect at dosage levels where it does not elevate triglyceride levels above the normal range."

Biesalski describes aerosol formulations containing ATRA (retinoic acid) for treating disorders of mucous membranes. Given that Belloni teaches away from using ATRA in his gels, ointments, and creams, one of skill would not look to modify Biesalski's aerosol (which contains ATRA) to the gel, ointment, or cream described by Belloni. Again, this is because Belloni found that ATRA elevates triglyceride levels when administered in amounts effective to repair damaged mucosa.

In view of the above, obviousness has not been established, and withdrawal of the rejection of claims 1-8, 11, 12, and 21 under 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request entry of the present Amendment and allowance of the amended claim set provided herein. The

Examiner is encouraged to phone Applicants' attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

Davis Wright Tremaine LLP
1201 Third Avenue, Suite 2200
Seattle, Washington 98101-3045
Telephone: 206-757-8023
Facsimile: 206-757-7023

Respectfully submitted,
Mendy S. MACABEE et al.
Davis Wright Tremaine LLP

/Barry L. Davison, Ph.D., J.D./
Barry L. Davison, Ph.D., J.D.
Attorney for Applicant
Registration No. 47,309